

**REMARKS/ARGUMENTS**

The following remarks and arguments are submitted in response to the Office Action mailed August 29, 2005. Claims 13-36 are pending in the application. Claims 13-26 stand rejected. In view of the remarks and arguments presented below, Applicant believes that the rejections have been overcome and respectfully requests reconsideration of the application, withdrawal of the outstanding rejections, and allowance of the claims.

**Request for Withdrawal of Final Rejection**

The Examiner has issued a final rejection of claims 13-36. Applicant respectfully submits that the finality of the rejection is premature and improper, and requests that the Examiner reconsider and withdraw the finality of the rejection. The finality of the rejection is premature because “new” grounds of rejection have been asserted. In the present Office Action, the Examiner has rejected claims based upon new prior art not previously relied upon (Mathies et al.) – a new ground of rejection –, and has also reintroduced rejections and prior art that were previously withdrawn – also new grounds of rejection. Although the same grounds of rejection and same prior art were previously asserted by the Examiner, the Examiner expressly acceded to Applicant’s arguments against the rejections and amendments, and withdrew the rejections. In view of the fact that these rejections were previously withdrawn, the reintroduction of the rejections now makes them “new” grounds of rejection.

The MPEP specifically provides that a final rejection of a second office action shall not be made final “where the examiner introduces a new ground of rejection that is [not] necessitated by Applicant’s amendment of the claims” or “if it includes a rejection, on prior art not of record, of any claim amended to include limitations which should reasonably have been expected to be claimed.” MPEP §706.07(a).

In the Office Action dated January 14, 2004, the Examiner rejected all claims under 35 U.S.C. §102(e), as being anticipated by Jordan (US 6,017,699, filed March 29, 1996) or Vasta et al. (US 6,326,485), as well as under 35 U.S.C. §103(a), as being obvious in view of Ruano (US 5,427,911) in combination with Rao (Analytical Biochem.216:1-14, 1994) and Ahern (The Scientist 9(15):1-5, 1995). Applicant responded to the rejection by amending the claims to

clarify that the “sequencing reagents” were combined in a “mixture” in a “single reaction vessel” (rather than a single shipping container, as suggested by the Examiner) and by distinguishing over the cited prior art. In response to the Applicant’s above arguments and amendments in the Office Action dated January 1, 2005, the Examiner *withdrew* all of the above rejections, issued a new rejection of all claims under 35 U.S.C. §112 and a rejection under 35 U.S.C. §103(a), on grounds of obviousness in view of Mian et al. (US 5,683,657), in combination with Ahern. In response to this rejection, Applicant amended the claims again to further clarify that the claimed kits comprised a reaction vessel “for each DNA region to be sequenced” and that the reagents were “for sequencing the sense and anti-sense strand” of each DNA region to be sequenced. In the most recent office action, dated August 29, 2005, the Examiner *withdrew* all of these rejections, but now inexplicably reverts back to the same references and same arguments previously relied upon in the rejection in the January 14, 2004, Office Action, which the Examiner also previously *withdrew*!, with the sole exception of a single new reference, Mathies et al.

The present Office Action first rejects claims 13-16 and 25-28 under 35 U.S.C. §102(e), as being anticipated by Jordan (US 6,017,699). This same rejection, based on the same arguments, was previously made by the Examiner in the January 14, 2004, Office Action, and is now repeated in the present Office Action, virtually verbatim. In view of the fact that this same prior art and the same reasoning were propounded and then withdrawn by the Examiner in a previous Office Action, Applicant submits that this constitutes a new grounds of rejection, making the finality of the present office action improper. Because the Examiner withdrew the previous grounds of rejection expressly “in view of Applicant’s amendment of the claims” and the arguments made by the Applicant, the Examiner manifestly acceded to these previous amendments and arguments, including the argument that Jordan does not disclose the elements of the claimed invention. To the extent the Examiner now wishes to reintroduce these same grounds of rejection previously withdrawn, Applicant presumes that the Examiner is relying on a new argument or new grounds of rejection not previously made. No such argument, however, is articulated in the present Office Action. In this regard, Applicant notes that the Examiner states that this new rejection based on Jordan was “necessitated by Applicant’s amendment of the claims”; however, no explanation or reasoning is provided why the amendments – which merely clarified and did not expand the scope of the claims – now justify the resurrection of a previously

withdrawn rejection. Indeed, the only new limitations that were added to the claims in subsequent amendments were those underlined below

13. A kit for sequencing one or more DNA regions from a genomic DNA sample or a microorganism, said kit consisting of, in packaged combination, a single reaction vessel for each DNA region to be sequenced containing a mixture of region-specific sequencing reagents sufficient for sequencing the sense and anti-sense strand of each DNA region to be sequenced and optionally in said mixture one or more non-region specific sequencing reagents, wherein said region-specific sequencing reagents comprise region-specific primers, and said optional non-region specific sequencing reagents are selected from one or more of the group consisting of deoxynucleotide triphosphate feedstocks, at least one chain terminating dideoxynucleotide triphosphate and a thermally stable polymerase enzyme capable of incorporating dideoxynucleotides into an extending nucleic acid polymer.

None of the above new limitations in any way constitute subject matter that raise any new issues or “necessitate” a new rejection based on prior art that the Examiner previously agreed did not anticipate. If Jordan did not previously anticipate the earlier claims, it is not possible that they anticipate the above claim, which contains all of the elements previously recited, plus additional limitations. In short, because the Examiner previously agreed that Jordan did not anticipate the claims and then withdrew the rejection based on Jordan, the reintroduction of Jordan constitutes a “new” ground of rejection, which should preclude a final rejection. Applicant respectfully submits that the most recent amendments do not “necessitate” the new rejections, and the final rejection should be withdrawn.

The present Office Action also rejects claims 13, 17-25 and 29-36 under 35 U.S.C. §103(a), as being obvious in view of Mathies et al. (US 5,707,804), in combination with Ruano (US 5,427,911) Rao (*Analytical Biochem.*216:1-14, 1994) and Ahern (*The Scientist* 9(15):1-5, 1995). In comparing the office action dated January 14, 2004, and the present office action dated August 29, 2005, the grounds of rejection are essentially identical. Indeed, the Examiner’s arguments with respect to the Ruano, Rao and Ahern references are virtually verbatim the same. The present Office Action, however, also relies upon Mathies, a newly cited reference not previously cited by the Examiner, making this rejection a new grounds of rejection.

In summary, having once acceded to Applicant’s argument and withdrawn the basis of the previous rejection, the Examiner cannot now reintroduce the grounds of rejection without providing some explanation or rationale. The Examiner’s mantra that “the new grounds of

rejection [were] necessitated by Applicant's amendment of the claims" cannot be invoked without providing Applicant with some explanation or rationale why Applicant's amendment "necessitated" the new rejection, indeed, why the amendment "necessitated" reintroducing a rejection that had previously been made, addressed and withdrawn. Applicant's recent amendment merely clarifies, without enlarging, the scope of the claims, and does not give rise to any alteration in the scope of the claims that could not previously have been relied upon by the Examiner in support of the same rejection. Although Applicant acknowledges that the examiner has the right to reintroduce the same grounds of rejection previously made and withdrawn, Applicant submits that such action requires some explanation why the Examiner is reneging on her previous acquiescence with Applicant's prior arguments. More significantly, the Examiner is obligated to clearly and particularly identify and differentiate the subject matter that supposedly now "necessitates" the new rejection from the subject matter the Examiner previously found to be acceptable. At the very least, the Examiner should withdraw the finality of the rejection so as to provide Applicant with fair opportunity to respond to this surprise last-minute maneuver that inexplicably raises issues that both the Examiner and Applicant had previously resolved and put to rest.

#### **Claim Rejections Under 35 USC § 102**

In view of the impropriety of the final rejection, and in an effort to expedite prosecution, Applicant will also address the substance of the prior art rejections. Claims 13-16 and 25-28 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Jordan, U.S. Patent No. 6,017,699. The Examiner specifically argues that Jordan teaches a kit with a single reaction vessel (microtitre plate) for each DNA region to be sequenced, in mixture with primers for sequencing both the sense (coding) and antisense (non-coding) strands of each region of genomic DNA. Applicant respectfully traverses the Examiner's rejection on grounds that the Examiner's characterization of Jordan is factually incorrect and does not therefore anticipate the claims.

First, Applicant notes that this same rejection was previously made by the Examiner in the Office Action dated January 14, 2004, argued over by Applicant in a response dated July 7, 2004, and withdrawn by the Examiner in the Office Action dated January 1, 2005, based on Applicant's amendment and arguments. In Applicant's July 7, 2004, response, Applicant argued that the claims of the present invention require that the kit contain "a single reaction vessel for

each DNA region to be sequenced containing a mixture of region-specific sequencing reagents sufficient for sequencing the sense and anti-sense strand of each DNA region to be sequenced.” Applicant further pointed out that the kit of Jordan does not contain these limitations. Jordan does not disclose a “single reaction vessel” containing a “mixture” of reagents for sequencing both the sense and anti-sense strand of each DNA region to be sequenced. Rather, Jordan teaches that the kit contains a “microwell plate” with “probes” (column 7, line 7-8) for an “ssDNA” (i.e., single strand DNA). Clearly, a single strand DNA cannot include both a sense and antisense strand. The Examiner has cited to column 10, line 7-17, for the proposition that the reaction vessel contains primers for both the sense and antisense strands, but the cited language relied on by the Examiner does not teach this. Rather, this section in Jordan teaches that “one primer must hybridize to one strand of DNA, and the other must hybridize to the opposite strand,” which merely states the well-known fact that in PCR amplification, primers anneal to separate strands. Nowhere does Jordan teach or suggest that these primers are combined in a single reaction mixture. In fact, Jordan teach the opposite – that primers are combined in separate reaction vessels. At column 17, lines 44-54, Jordan states that the “captured single strand of DNA [is] available for probe hybridization, and the “single-stranded . . . DNA probe is added to the wells containing the captured single-stranded amplimer.” Thus, the sense and antisense strands are separated, the reaction vessel contains only a single-stranded DNA, and the reaction vessel clearly does not contain sufficient reagents to sequence both the sense and anti-sense strands. In view of the clear distinctions between Jordan and the claimed invention, Jordan does not anticipate the claimed invention, and this ground of rejection should be withdrawn.

### **Claim Rejections Under 35 USC § 103**

The Office Action further rejects claims 13, 17-25 and 29-36 under 35 U.S.C. § 103(a) as being unpatentable over Mathies et al. (U.S. Patent No. 5,707,804) and Ruano (U.S. Patent No. 5,427,911) in view of Rao (Analytical Biochemistry, vol. 216, pages 1-14 (1994)) and further in view of Ahern (The Scientist, Vol. 9, No. 15, pages 1-15 (June 1995)). Applicant respectfully traverses this rejection, for the reasons explained below.

M.P.E.P. 706.02(j) sets forth the standard for a Section 103(a) rejection:

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or combine reference teachings. Second, there must be a reasonable expectation of success. Finally, **the prior art reference (or references when combined) must teach or suggest all the claim limitations.** The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). (Emphasis added).

The 35 U.S.C. §103(a) obviousness rejections of claims 13, 17-25 and 29-36 are improper because the Examiner has not explained how the cited references teach or suggest all the claim limitations. As noted above, the Examiner previously withdrew a §103(a) obviousness rejection based on the Ruano, Rao and Ahern references. Applicant specifically argued that Rao teaches use of radiolabeled primers that must be separated in different reaction vessels, that Ruano et al. teach a plurality of reaction vessels and fails to teach that the reagents for both sense and antisense strands are mixed in the same reaction vessel, and that Ahern merely describes the general concept of a kit, without and details pertinent to the claimed invention. The Examiner agreed with the above arguments, and withdrew the rejection. The Examiner has not raised any additional arguments in respect of these references, and has not provided Applicant with any explanation why these references, which the Examiner previously agreed did not teach or suggest the elements of the present invention, now render the claimed invention obvious. If the Examiner has officially acknowledged that prior art does not render the claims obvious, and then elects to reverse that determination, Applicant is entitled to a detailed explanation of the reasons for doing so.

The Examiner now reasserts these same references – Ruano, Rao and Ahern – in the current rejection, combined with the additional reference of Mathies. With respect to Mathies, the Examiner cites to column 10, lines 26-62 and column 14, lines 12-26 in support of the rejection, yet acknowledges that Mathies teach a method for copying “single stranded DNA fragments.” At column 14, lines 12-26 (claim 8 of Mathies), the method expressly recites “primers for copying a single stranded nucleic acid.” Mathies thus fails to teach reagents in a single reaction vessel capable of sequencing both sense and anti-sense strands of genomic DNA. Neither do any of Ruano, Rao or Ahern compensate for or provide any teaching or suggestion of

this element of the claimed invention. Indeed, not a single one of these references teach any of the limitations of a single reaction vessel containing a mixture of reagents capable of sequencing both the sense and antisense strands of a DNA template. For these reasons, the combination of Mathies, Ruano, Rao and Ahern fail to teach or suggest the present invention. Applicant respectfully requests that the outstanding rejections based on these references be withdrawn, and the claims allowed.

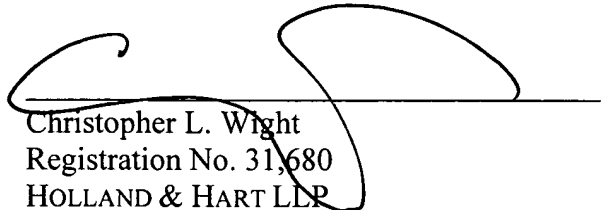
### **CONCLUSION**

In summary, Applicant respectfully submits that the final rejection is premature, and that the grounds of rejection articulated by the examiner are new grounds of rejection that were either previously made and withdrawn (the §102(e) rejection based on Jordan) or that are based on newly cited prior art not previously asserted by the examiner (the §103(a) rejection based in part on newly cited Mathies reference). In either case, Applicant submits that the renewed reliance on references previously distinguished over and acceded to by the Examiner is improper, or at least warrants some explanation on the part of the Examiner and opportunity for Applicant to respond. The finality of the rejection should therefore be withdrawn to allow Applicant fair opportunity to address the new issues raised by the Examiner.

Furthermore, with respect to the substantive merits of the prior art rejections, Applicant has demonstrated that the references fail to teach or suggest each and every element of the claimed invention.

Applicant submits that the claims define subject matter that is neither taught nor suggested by the cited references. For the above reasons, Applicant respectfully requests that the claims of the application be allowed and proceed to issuance.

Respectfully submitted,



Christopher L. Wight  
Registration No. 31,680  
HOLLAND & HART LLP  
P.O. Box 11583  
Salt Lake City, UT 84147-0583  
Telephone: (801) 595-7823  
Fax: (801) 364-9124

CLW/jml  
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